



The relationship between vitamin D And human papilloma virus infection

D vitamini ve human papilloma Virüs enfeksiyonu ilişkisi

Vitamin D and hpv infection

Cuma Mertoğlu¹, Ümit Nayır², Cenk Nayır², Murat Günay¹
¹Clinical Biochemistry, ²Obstetrics and Gynecology,
Erzincan University Faculty of Medicine, Erzincan, Turkey

Öz

Amaç: D vitamini eksikliği ve hastalıklarla ilişkisi son dönemlerde üzerinde çok çalışılan önemli bir halk sağlığı sorunudur. Human papilloma virüsü (HPV) genital enfeksiyonu cinsel yolla bulaşan enfeksiyonlardan en yaygın rastlanlarından biridir. Bu çalışmada D vitamini ve HPV enfeksiyonu ilişkisini araştırdık. Gereç ve Yöntem: Yaşları 30- 45 yıl arası, HPV pozitif olan 68 kadın ve HPV negatif olan sağlıklı 30 kadın olmak üzere bireyler iki gruba ayrıldı ve serum D vitamini düzeyleri kıyaslandı. Bulgular: HPV enfeksiyonu pozitif grup ile HPV enfeksiyonu negatif olan kontrol grubu arasında serum D vitamini düzeyleri açısından fark yoktu (Sırasıyla, ortalama \pm SD; 13.7 \pm 6.9, 13.3 \pm 5.2), p=0.804). Ancak her iki grupta da yaygın D vitamini eksikliği [20 ng/ml'nin altında, HPV (+) grupta %82,4, HPV (-) grubunda ise %83,4] vardı. Tartışma: Ülkemizde genç kadınlarda D vitamini eksikliği çok yaygındır. D vitamini eksikliği HPV enfeksiyonu ile ilişkili bulunmamıştır.

Anahtar Kelimeler

D Vitamini; Human Papilloma Virüsü; Serviks Kanseri; Genital Enfeksiyon; Cinsel Yolla Bulaşan Enfeksiyonlar

Abstract

Aim: Vitamin D deficiency and its relationship with diseases have been an important public health problem that has been studied very much in recent years. Human papilloma virus (HPV) is one of the most common diseases that cause genital infections from genital infections. In this study, we investigated the relationship between vitamin D and HPV infection. Material and Method: Between the ages of 30 and 45 years, 68 women with HPV positive and 30 healthy women with HPV negative were divided into two groups and serum vitamin D levels were compared. Results: There was no difference in serum vitamin D levels between the HPV infection positive group and the HPV infection negative group (mean \pm SD, 13.7 \pm 6.9, 13.3 \pm 5.2), p = 0.804). However, both groups had widespread D vitamin deficiency (less than 20 ng/ml, 82.4% in the HPV (+) group and 83.4% in the HPV (-) group). Discussion: Vitamin D deficiency is very common in young women in our country. Vitamin D deficiency was not associated with HPV infection.

Keywords

Vitamin D; Human Papilloma Virus; Cervical Cancer; Genital Infections; Sexually Transmitted Infections

DOI: 10.4328/JCAM.5400

Received: 25.09.2017 Accepted: 19.10.2017 Printed: 01.11.2017

J Clin Anal Med 2017;8(6): 538-40

Corresponding Author: Cuma Mertoğlu, Biyokimya Laboratuvarı, Mengücek Gazi Eğitim ve Araştırma Hastanesi, Merkez, Erzincan, Türkiye.

GSM: +905066377725 E-Mail: drcumamert@hotmail.com

Introduction

Human papilloma virus (HPV) genital infection is one of the most common sexually transmitted infections worldwide [1]. HPV infection may be asymptomatic, also may cause genital warts, cervical precancer or cancer [2]. Approximately 40 different HPV types have been categorized, some of which are considered high risk (HPV 16, 18, 31, 33) and some are low risk (6, 11, 40, 42) in terms of the carcinogenic potential of the cervix [3]. High-risk HPVs are associated with precancerous lesions leading to cervical cancer such as cervical dysplasia or cervical squamous intraepithelial lesions (SIL) [4]. Nearly all cervical malignancies (99.7%) and about 40% of vaginal cancers are caused by HPV [5].

In the last decade, the lack of vitamin D and its deficiency related to diseases have become a major public health issue [6]. While adequate vitamin D levels protect against some infectious diseases, vitamin D deficiency is associated with increased risk and severity of illness. For example, upper and lower respiratory tract infections (e.g., influenza and respiratory syncytial virus infection) are inversely proportional to serum 25 (OH) D level, and these infections peak during the winter months when vitamin D deficiency increases [7]. Furthermore, low serum 25 (OH) D levels were associated with increased risk of active tuberculosis, while high levels were found to accelerate tuberculosis recovery [8]. In a study conducted in American women, vitamin D levels were inversely related to the prevalence of HPV infection [9].

When vitamin D deficiency and its relationship with infections were considered, we have seen that there are not many studies investigating the relationship between HPV infection and vitamin D, and we have carried out this study.

Material and Method

Between 2016 December and 2017 April, 98 sexually active women who applied to our hospital, department of obstetrics and gynecology for routine control were included in this study. Participant women were aged 30-45 and have regular menstrual periods. A pelvic examination including visual, bimanual and ultrasonographic evaluation was performed on all subjects. Cervical smears were obtained from all subjects. Pap smears were classified according to Bethesda's cervical cytology reporting system in 2001 [10]. All of the cases were cytologically normal (Bethesda Class 1) and not accompanied by other genital infections, previously cervical lesions and cervical cancer history. All HPV-positive individuals were asymptomatic. Individuals who use birth control pills, who had an infection within the last three months in the genitourinary system or in any part of the body such as the upper respiratory system, individuals with any malignant tumors and who use any medications are not included in the study. 68 female subjects who were HPV positive and 30 female subjects who were HPV negative were divided into two groups. The colposcopic evaluation was performed on cases that were evaluated as positive for HPV infection, and as a result, normal subjects were taken to work. All transactions carried out in this work have been carried out in accordance with the ethical standards of the institutional and / or national research committee and the 1964 Helsinki Declaration and subsequent

amendments or comparable ethical standards. All subjects gave written informed consent for participation in the study, which was approved by local ethics committee.

The blood from the peripheral venules was centrifuged, and the serum was separated and stored at -80 ° C until the day of operation. Serum vitamin D level was measured by Siemens Centaur XP (Siemens Healthcare, Diagnostics Products Ltd., London, UK) using chemiluminescence immunometric method.

Statistical analysis

Statistical analysis was performed using the SPSS 18.0 (SPSS Inc., Chicago, IL) program. Control of normality distributions after the Kolmogorov Smirnov test, the t-test was used for intergroup comparisons. $P < 0.05$ was considered significant.

Results

There was no difference in the serum vitamin D levels between the HPV infection positive group and the HPV infection negative control group ($p=0.804$) (Figure 1). However, both HPV (+) group and the control group had vitamin D deficiency (Table 1). 82.4% in the HPV (+) group and 83.4% in the control group had a vitamin D level below 20 ng/ml. The mean age of the HPV positive group was 36.72 ± 4.5 , and the control group was 36.90 ± 4.3 , and there was no difference between the two groups.

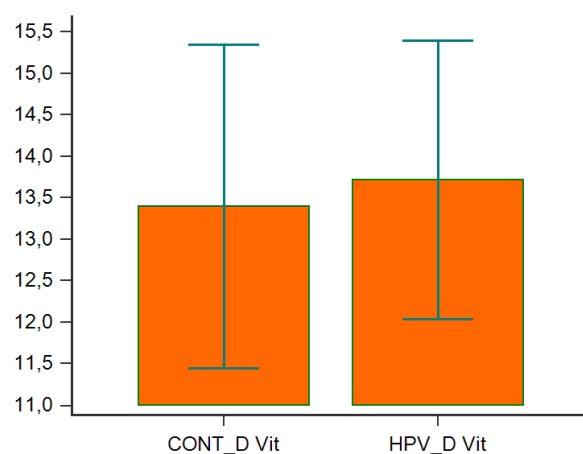


Figure 1. Mean and distribution of serum vitamin D in the control group and HPV (+) group.

Table 1. Comparison of serum vitamin D levels between groups.

Parameter	Group	n	Mean	Standard deviation	95 % CI	Minimum	Maximum	p value
Vitamin D (ng/ml)	HPV (+)	68	13.7	6.9	12.0-15.3	4.2	34.2	0.804
	HPV (-)	30	13.3	5.2	9.9-16.2	5.9	25.1	

Abbreviations: CI: Confidence interval, HPV: Human papilloma virus.

Discussion

This study showed that both HPV (+) women (82.4%) and HPV (-) healthy young women (83.4%) are suffering from severe vitamin D deficiency in our country. According to the 14th International Conference on Vitamin D Workshop Consensus Conference held in Belgium in October 2009, it was suggested that the minimum desired serum 25 (OH) D level was 20 ng/ml [11]. For this reason, we also determined the cut-off value of 20 ng/

ml for the adequate level of vitamin D in our study. This is the first study to investigate vitamin D level and HPV association in the Turkish population. There was no difference in vitamin D levels among individuals who were HPV infection positive and negative. However, encountering severe vitamin D deficiency in both groups may have prevented this relationship from being revealed. As a matter of fact, in a study conducted in American society, the seroprevalence of cervicovaginal HPV was found to be associated with low D vitamin levels. Because in this study the proportion of individuals with vitamin D levels below 20 ng/dl was 30.5 % [9]. Therefore, in our society, vitamin D is added to all women, and when the level has reached an adequate level, the seroprevalence of HPV can be evaluated again. Our results are similar to the study conducted in a group of patients with systemic lupus erythematosus that vitamin D level was not associated with HPV positivity [12].

Previous studies have shown that low levels of vitamin D are associated with bacterial vaginosis and chlamydial infection [13,14]. Although clinical evidence has shown vitamin D supplements to reduce susceptibility to respiratory syncytial virus infection in vitro studies, have not shown that vitamin D reduces virus replication in epithelial cells [15]. However, studies have shown effects of vitamin D on expression and secretion of proinflammatory cytokines and chemokines [16]. The variety of these effects indicates that vitamin D is more effective on some pathogens than some other pathogens [17].

In a study conducted in our country, vitamin D deficiency was found as 27.8 % in İzmir and 76.3 % in Erzurum province. [18]. In our study, vitamin D deficiency (≤ 20 ng/ml) was found as 82.4 % and 83.4 %. This result is similar to the results of the study in the province of Erzurum, which has similar climatic characteristics and is located near the local region. Both results indicate that vitamin D deficiency is more common in cold and low sun areas. In another study, vitamin D deficiency in the Ankara region was found as 72.5 % [19].

One reason for the low level of vitamin D in this study is that samples are collected during the winter and spring seasons when sunlight is low. It is known that the level of vitamin D is seasonally different [7,18]. Another limitation of this study is that partly a small number of participants.

As a result, vitamin D deficiency is common in young women. Therefore, it is important for this group to take Vitamin D supplementation. In this study which we investigated the HPV association of vitamin D, we found no difference between groups because vitamin D deficiency was common in all groups. A similar study should be repeated after an adequate level of vitamin D has been obtained.

Competing interests

The authors declare that they have no competing interests.

References

1. Carter JR, Ding Z, Rose BR. HPV infection and cervical disease: a review. *Aust. N. Z. J. Obstet. Gynaecol.* 2011;51:103–8.
2. Wright TC, Richart RM. Role of human papillomavirus in the pathogenesis of genital tract warts and cancer. *Gynecol Oncol.* 1990;37(2):151–64.
3. Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, et al. A review of human carcinogens-Part B: biological agents. *Lancet Oncol.* 2009;10:321–2.
4. Trottier H, Franco EL. The epidemiology of genital human papillomavirus infection. *Vaccine.* 2006.
5. Walboomers JMM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, et al.

Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J. Pathol.* 1999;189:12–9.

6. Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, et al. The 2011 Dietary Reference Intakes for Calcium and Vitamin D: What Dietetics Practitioners Need to Know. *J. Am. Diet. Assoc.* 2011;111:524–7.

7. Juzeniene A, Ma LW, Kwitniewski M, Polev GA, Lagunova Z, Dahlback A, et al. The seasonality of pandemic and non-pandemic influenzas: The roles of solar radiation and vitamin D. *Int. J. Infect. Dis.* 2010;14.

8. Sita-Lumsden A, Laphorn G, Swaminathan R, Milburn HJ. Reactivation of tuberculosis and vitamin D deficiency: the contribution of diet and exposure to sunlight. *Thorax.* 2007;62:1003–7.

9. Shim J, Pérez A, Symanski E, Nyitray AG. Association between Serum 25-Hydroxyvitamin D Level and Human Papillomavirus Cervicovaginal Infection in Women in the United States. 2016;213:1886–92.

10. Nayar R, Wilbur DC, Solomon D. The Bethesda System for Reporting Cervical Cytology. *Compr Cytopathol.* 2008; 77–90.

11. Henry HL, Bouillon R, Norman AW, Gallagher JC, Lips P, Heaney RP, et al. 14th Vitamin D Workshop consensus on vitamin D nutritional guidelines. *J. Steroid Biochem. Mol. Biol.* 2010;121:4–6.

12. García-Carrasco M, Mendoza-Pinto C, Munguía-Realpozo P, Rodríguez-Gallegos A, Vallejo-Ruiz V, Muñoz-Guarmos M, et al. Lack of association between serum 25-hydroxyvitamin D levels and cervical human papillomavirus infection in systemic lupus erythematosus. *Lupus.* 2015;24:606–12.

13. Hensel KJ, Randis TM, Gelber SE, Ratner AJ. Pregnancy-specific association of vitamin D deficiency and bacterial vaginosis. *Am. J. Obstet. Gynecol.* 2011;204.

14. He Q, Ananaba G a, Patrickson J, Pitts S, Yi Y, Yan F, et al. Chlamydial infection in vitamin D receptor knockout mice is more intense and prolonged than in wild-type mice. *J. Steroid Biochem. Mol. Biol.* 2012;1–8.

15. Bergman P, Lindh AU, Björkhem-Bergman L, Lindh JD. Vitamin D and Respiratory Tract Infections: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *PLoS One.* 2013;8:1–9.

16. Greiller CL, Martineau AR. Modulation of the Immune Response to Respiratory Viruses by Vitamin D. *Nutrients.* 2015;7:4240–70.

17. Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y, Ida H. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. *Am. J. Clin. Nutr.* 2010;91:1255–60.

18. Gür EB, Turan GA, Tatar S, Gökdoğan A, Karadeniz M, Çelik G, et al. The effect of place of residence and lifestyle on vitamin d deficiency in pregnancy: Comparison of eastern and western parts of Turkey. *J. Turkish Ger. Gynecol. Assoc.* 2014;15:149–55.

19. Uçar F, Yavuz M, Taşlıpınar AÖ, Soydaş NÖ. Ankara Etlik İhtisas Eğitim ve Araştırma Hastanesine Başvuran Hastalarda 25-OH Vitamin D Düzeyleri. *Eur J Basic Med Sci.* 2012;2:12–5.

How to cite this article:

Mertoğlu C, Nayki Ü, Nayki C, Günay M. The Relationship Between Vitamin D and Human Papilloma Virus Infection. *J Clin Anal Med* 2017;8(6): 538-40.